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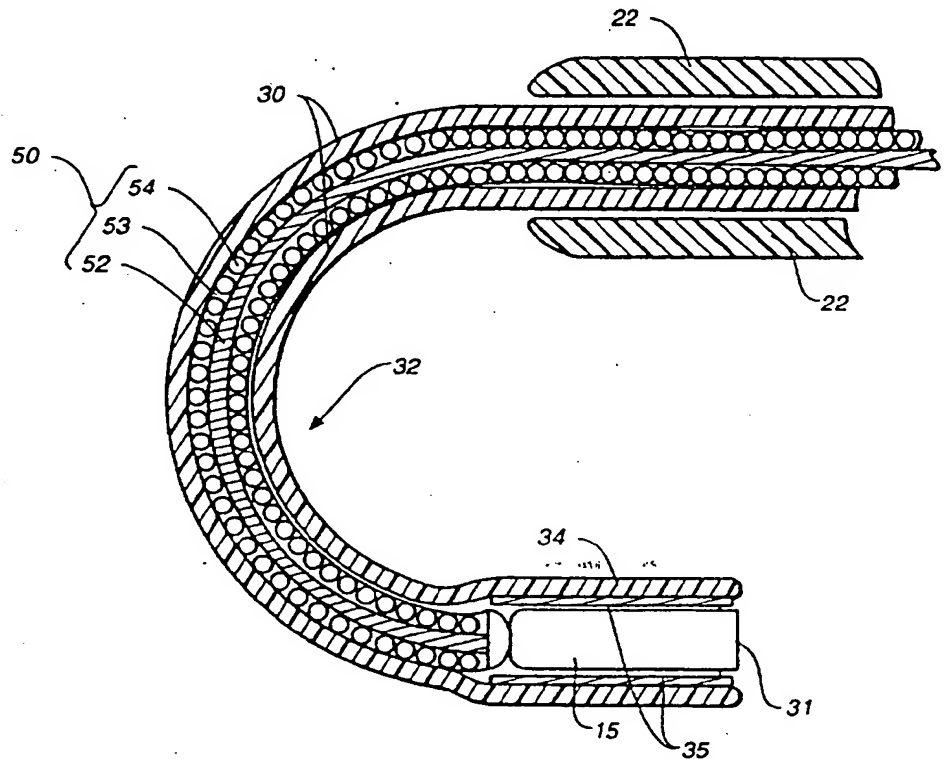
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(54) Title: EMBOLIZATION DEVICE

(57) Abstract

A device for delivery of an embolization plug (15) into a biological vessel includes a tubular sheath (22) assembly and a flexible catheter (30) disposed therethrough. The catheter has a front end section (32) which is semicircularly arcuate when unconstrained and holds an embolization plug (15) near its front opening. The catheter can be rotated inside a vessel from its back end and the curvature of the arcuate front end section can be varied as the distance by which it extends from the sheath assembly is adjusted. The plug is pushed forward out of the catheter by a push rod (50) which is disposed in the lumen of the catheter and has a flexible front part which can move through the catheter without significantly affecting the arcuate configuration of its front tip section.



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EMBOLIZATION DEVICE

Background of the Invention

This invention relates to a device for embolization of a biological vessel or other medical purposes.

- 5 More particularly, this invention relates to a medical device and a procedure for delivering a plug-like material into a body cavity for occlusion or for depositing drugs.

- Embolization is defined as any procedure which
- 10 reduces blood flow by obstruction. There is a great variety of clinical situations where blood vessels must be blocked, such as when bleeding in the brain needs to be controlled or when the blood supply to tumorous tissues must be blocked. Other examples of
- 15 situations requiring permanent or temporary embolization include, but are not limited to, occlusion of saphenous vein side branches in a saphenous bypass graft procedure, neurovascular occlusion, chemoembolization, aortic aneurysm
- 20 correction procedure, chronic venous insufficiency treatment, and renal embolization.

- Various means have been used in these applications to occlude blood vessels, such as by advancing a small diameter catheter from a distant vessel, inflating a
- 25 small rubber balloon at the end of the catheter to mechanically wedge it into place in order to block

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the vessel, and thereafter withdrawing the catheter. A disadvantage of this method is that the rubber balloon may become dislodged at a later time and become life-threatening as a free-floating embolus.

5 Another procedure is to inject at the desired site in the blood vessel a suspension of collagen with clotting factors, thereby inducing an embolus. The clots will be re-absorbed with time, alleviating the risk of a free-floating embolus. This procedure,

10 however, is not desirable when precise location of the embolus is desired because the clotting must be induced sufficiently rapidly such that the clot can be prevented from moving downstream to an undesired location or from forming microemboli before attaching

15 to the blood vessel walls. Still another procedure, which has been suggested, is to use a syringe to inject through a catheter a liquid suspension of particles or small "pledgets" manufactured from animal gelatin, but the use of a syringe to inject

20 suspended particles into a catheter limits the compression of the particles and the resultant mechanical fixation in-situ of the embolizing material. In view of the above, U.S. Patent Application Serial No. 07/948,235 filed September 21,

25 1992 (assigned to the present assignee and herein incorporated by reference) disclosed embolization plugs which may be characterized as comprising one or two pieces of flexible and deformable sponge-like collagen material, capable of being compressed to be

30 inserted into a tubular biological vessel such as a blood vessel. Such plugs can also absorb fluid, after they are inserted into a vessel, to expand so as to provide mechanical fixation inside the vessel and also to block the flow of fluid such as blood

35 through the vessel. Another advantage of such plugs is that they can contain antibiotics or other kinds of drugs which may be desirable at the position of

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the vessel where they are deposited. In other words, such plugs can serve not only for occlusion of a vessel but also as a carrier of drugs.

It is therefore an object of this invention to
5 provide a device for accurately and reliably delivering such a plug to a desired part of a body cavity for occlusion or for depositing drugs.

Summary of the Invention

A device embodying the present invention, with which
10 the above and other objects can be accomplished, may be characterized as comprising a tubular sheath assembly, a flexible catheter disposed therethrough for loading an embolization plug near its front opening, and a deployment assembly for pushing the
15 loaded plug out of the catheter through its front opening. The catheter has a front tip section which is semicircularly arcuate like a hook, when in an unconstrained condition. As the catheter is moved longitudinally through the sheath so as to vary the
20 distance by which the tip section protrudes forward from the sheath assembly, however, the curvature of the tip section, and hence also the direction in which the front opening of the catheter points, can be adjusted. The catheter is sufficiently resilient
25 such that it can reliably translate a torque exerted at its back end to the tip section. Thus, a user can maneuver the back end of the catheter to direct its front tip into a selected branch vessel, say, while watching the process through an angioscope. The plug
30 is preferably made from a bioresorbable material such as collagen, and is pushed forward out of the catheter by means of a push rod disposed in the lumen of the catheter. The push rod has a flexible front part capable of moving through the arcuate tip

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section of the catheter without significantly affecting its curved configuration.

Brief Description of the Drawings

The accompanying drawings, which are incorporated in
5 and form a part of this specification, illustrate an
embodiment of the invention and, together with the
description, serve to explain the principles of the
invention. In the drawings:

10 Fig. 1 is a side view of a device embodying the
present invention;

Fig. 2 is a sectional side view of the sheath
assembly of the device of Fig. 1;

Fig. 3 is a sectional side view of the frontal end
parts of the device of Fig. 1;

15 Figs. 4A and 4B are sectional side views of the
frontal end parts of Fig. 3, showing how the
curvature of the catheter changes as the distance by
which it protrudes from the front opening of the
sheath assembly is changed;

20 Fig. 5 is a sectional side view of a front part of
the deployment assembly of the device of Fig. 1,
including its T-connector;

Fig. 6 is a sectional side view of a back part of the
deployment assembly of the device of Fig. 1,
25 including the plunger body;

Fig. 7 is a sectional view of an alternative sheath
assembly embodying the invention;

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Figs. 8A, 8B and 8C are sectional views of the frontal end parts of the device of Fig. 1 according to alternative designs;

Fig. 9 is a perspective view of the front end section
5 of another catheter embodying the present invention;
and

Figs. 10A and 10B are sectional views taken along line 10-10 in Fig. 9 respectively when the plug is behind its slit valve and when it is being pushed out
10 of the catheter.

Detailed Description of the Preferred Embodiments

Fig. 1 shows a device 10 embodying the present invention, characterized as comprising a sheath assembly 20, a catheter 30 and a deployment assembly
15 40. Broadly described, the catheter 30 is for holding near its front opening 31 a plug (shown at 15 in Fig. 3) to be delivered into a biological vessel, the sheath assembly 20 is for locating the device 10 near the target position where the plug is intended
20 to be deposited, and the deployment assembly 40 is for pushing the plug out of the catheter 30. The device 10, as well as its three major components described above, is generally elongated. For the convenience of description, end parts of these
25 components, in the direction of which the device 10 is inserted into a patient's body, will be herein referred to as the distal or front end parts. Similarly, the opposite end parts, which are usually handled by the user, will be referred to as the
30 proximal or back end parts.

As briefly described above, the sheath assembly 20 is primarily for the purpose of locating the front opening 31 of the catheter 30 near the position where

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the plug is intended to be deposited. For this reason, the sheath assembly 20 is basically tubular, or comprised of tubular components having a longitudinally extending inner passage through which the catheter 30 is extended. As shown more in detail in Fig. 2, a sheath assembly according to a preferred embodiment of the invention may comprise a hemostasis fitting 21 and a Touhy-Borst connector 24. The hemostasis fitting 21 has a forwardly extending sheath tubing 22 bonded to its distal end and a female luer lock on the proximal end, and serves to prevent air from entering the parent vessel and pressurized blood from leaking out of the proximal end of the sheath assembly 20. The Touhy-Borst connector 24 is for the purpose of providing a tight grip around the catheter 30, thereby locking it in position with respect to the sheath assembly 20 by a quarter turn thereof. For this purpose, the Touhy-Borst connector 24 has a casing with a male luer end, a silicone sleeve and a cap such that, when the cap is tightened, the silicone sleeve is compressed and its inner diameter decreases to provide a tight grip around the catheter 30. The male luer end threads into the proximal end of the hemostasis fitting 21. The casing contains a duckbill valve 25 and has an irrigation port 26. The duckbill valve 25 is a check valve for keeping pressurized blood from flowing back through the annulus between the catheter 30 and the sheath assembly 20. It consists of a single component molded from an elastomeric material, and a slit at the end of its taper allows only a unidirectional flow. The irrigation port 26 is adapted to be connected to an irrigation line such that a stream of fluid can exit through an annular space between the sheath tubing 22 and the catheter 30 to thereby clear blood or the like out of the field of vision, for example, of an angioscope.

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The catheter 30 is basically an elongated tube made of a flexible material such as polyurethane, polyethylene, polypropylene, nylon, polyvinyl chloride, polyether block amide,

5 polyetheretherketone, or fluoropolymers with a naturally arcuate front end section 32 assuming a substantially semicircular shape, like a J-shaped hook, of radius about 1.6-6.4mm when it is under an unconstrained condition as shown in Fig. 3. The

10 tube may be a coextrusion or lamination of any of the above materials. It may be overbraided with polyamide, polyester or such reinforcing materials. It may also contain fibers, thread, wires, braid or such reinforcing material in order to enhance

15 torqueability and to prevent elongation when the deployment assembly 40 is activated. Since it is made of a flexible material, its curvature can be reduced as the catheter 30 is moved backwards (i.e., towards its proximal end) through the inner passage

20 of the sheath assembly 20 such that the arcuate front end section 32 begins to move into the sheath tubing 22, as shown in Figs. 4A and 4B. In other words, the curvature of the front end section 32 of the catheter 30, and hence the direction in which its front

25 opening 31 will point, can be adjusted by longitudinally moving the catheter 30 inside the inner passage of the sheath assembly 20.

As shown in Figs. 3, 4A and 4B, the plug 15 is positioned near the front opening 31 of the catheter

30 30, being held in a ferrule (or liner) 35, of which the inner surface has a reduced coefficient of friction such that the plug 15 can be easily pushed out. The ferrule (or liner) 35 may have a highly

35 polished surface or may be made of material with a low coefficient of friction such as metals or fluoropolymers. It may be coated with Teflon™ (E.I.

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Dupont), Hydrosil™ (TUA Systems), Polyslip™ (Union Carbide), propylene glycol, polyethylene glycol, silicone, or other such lubricious substances.

According to the embodiment of the invention shown in
5 Figs. 3, 4A and 4B, a lower durometer cylindrical tip
34 for holding the plug 15 is bonded or welded to the
front end of the arcuate front end section 32 of the
catheter 30. The forward end of the tip 34 is
softly beveled for ease of insertion, say, into a
10 side branch of a vein.

The deployment assembly 40 includes a T-connector 41,
a handle (or a flanged plunger barrel) 42, and a
plunger 43 at the proximal end part of the device 10,
as shown more in detail in Figs. 5 and 6. The T-
15 connector 41 is a tubular member with a side port 48,
and its female luer at its back end section is bonded
to a male luer of the handle 42. The side port 48 of
the T-connector 41 may serve as an irrigation port
for flushing dye contrast or heparinized saline
20 cleaning solution inside the catheter 30. The
proximal end of the catheter 30 is bonded to the
distal end of the T-connector 41. A seal 45 is
seated at a small distance in front of the female
luer end of the T-connector 41 and against the end of
25 the male luer of the handle 42, preventing liquid
from entering the back end portion of the deployment
assembly 40. The handle 42 has a transversely
protruding part (or a flange) for the ease of
handling even by a gloved hand. Although the
30 catheter 30 is made of a flexible and elastic
material, as mentioned above, it is sufficiently
rigid to have a reliably torque-communicating
property, or torqueability which means the ability to
translate the torque exerted by the user on the
35 proximal end in an even, predictable manner to the
tip section 32. The catheter 30 is also able to

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slide through the inner passage of the sheath assembly 20 with little or no resistance and is marked with indicator lines 33 on the J-shaped hook. In summary, the user can operate the handle 42 not only to change the distance by which the tip section 32 of the catheter 30 extends forward beyond the front end of the sheath tubing 22 to thereby control the direction of the front opening 31 but also to rotate the catheter 30 around its longitudinal axis so as to change the azimuthal angle of the arcuate tip section 32 of the catheter 30 in a well controllable manner.

As shown in Fig. 6, the plunger 43 is an elongated cup-shaped tubular member with a bottom 44 at its proximal extremity, engaging at its distal end with the proximal end part of the handle 42 and containing a biasing helical spring 46 inside. The distal end of the helical spring 46 is in contact with the proximal end of the handle 42, and its proximal end is in contact with the bottom 44 of the plunger 43 such that the plunger 43 as a whole can be pushed forward (towards the handle 42) against the biasing force of the spring 46 after it is rotated one eighth of a turn to disengage it from a cap lock mechanism (not shown), which serves to prevent unintentional deployment of the plug 15.

The deployment assembly 40 further includes a push rod 50 which is a flexible wire extending longitudinally and slidably through the lumen of the catheter 30. The proximal end of the push rod 50 is crimped and bonded into the material of the plunger 43. As shown more clearly in Fig. 3, the push rod 50 is composed of a core wire 52 of variable diameters along its length and a metal safety ribbon 53. Wire 54 is helically wound over the core wire 52

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and the safety ribbon 53. They are soldered together to form a guidewire-like unit. The distal end of the push rod 50 is sufficiently flexible so as not to significantly interfere with the arcuate configuration of the front end section 32 of the catheter 30 as it is pushed from behind to move forward therethrough. The push rod 50 can be coated with Teflon™ (E.I. Dupont), Hydrosil™ (TUA Systems), Polyslip™ (Union Carbide) or a similar lubricious material. As the push rod 50 is moved forward to deploy the plug 15, the helical spring 46 is compressed. As further shown in Fig. 6, the deployment assembly 40 is structured such that the plunger, and hence also the push rod 50, will not be able to advance forward by more than a predetermined maximum distance such that its distal end will be prevented from protruding from the front opening 31 of the catheter 30 and to thereby causing damage to the vessel. As soon as the plug 15 is deployed and the plunger 43 is released by the user, the compressed spring 46 serves to promptly retract the push rod 50.

The plug 15, according to one embodiment of the invention, is a single piece made from a collagen material. A collagen plug material is preferred because of its tissue compatibility and bioabsorption over time. It is also a very versatile material which can be formulated into a sponge, a film or a clear viscoelastic fluid, depending on the steps used in the processing. Collagen has some attractive chemical properties in vivo, such as being hemostatic, being chemotactic and encouraging fibroblast ingrowth. In implantation studies, it can provide a scaffold for healing deep wounds and formation of new tissue. The collagen material for the plug 15 may be of almost any commercially

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available type. It may preferably be from a processed animal source such as bovine corium (hide), bovine tendon and porcine skin. Reprocessed insoluble collagen from animal sources is

5 commercially available in the form of sponges or non-woven webs. The collagen is formed into the shape of plugs of appropriate size to be determined by the intended application. In an area of low venous throughput for temporary occlusion of blood flow, for

10 example, a plug which is not too much larger than the inner diameter of the vessel should suffice. For applications demanding permanent occlusion of vessels subjected to arterial pressures, on the other hand, a plug of higher compression modulus and larger

15 expanded size relative to the inner diameter of the lumen will be necessary. The shape of the plug can also be tailored to fit the need of a given application. A spherical, cylindrical, conical or rolled plug may be appropriate for any given

20 application.

Plugs can be molded or fabricated otherwise, and compressed into a given shape. Typically, the plugs are compressed sufficiently so that their diameter is

25 smaller than the lumen for ease of insertion. In general, such configurations that allow the most collagen to be inserted into the lumen are most beneficial. Sponge-like porous plugs with pore diameters greater than 50 microns are preferred for

30 promoting cellular ingrowth. A dry, highly compressed collagen plug like this fully hydrates and expands to several times its compressed size within a short period of time upon contact with bodily fluid, thereby tightly affixing itself to a particular

35 location within a blood vessel.

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The plug according to the present invention may be made from Collastat® Hemostatic Sponge (Vitaphore Corp.) Use may also be made of Vitacol™ (proprietary collagen of the assignee herein, very similar to Collastat in form and function), Semex Collagen Powder (Semex Medical, Inc.), etc. The crosslinking agent may be formaldehyde vapor (FMV), glutaraldehyde or other agents familiar to those skilled in the art. Crosslinking effectively increases the strength (compression modulus) of the material, and slows its bioerosion in vivo. Crosslinked collagen materials with shrink temperature ($= T_s$) greater than 55°C and with a modulus at 60% volumetric compression of greater than 0.15 g/mm² are particularly preferred.

Use may also be made of medical grade polyurethane foams such as Hypol (W.R. Grace & Co.) The urethane foams have very good memory characteristics and a higher compression modulus in water than a collagen sponge of similar solids content. Polyurethane plugs may be either impregnated with collagen or combined with aqueous collagen slurry in a foam-forming step. Plugs which are imbibed with collagen post foam-forming may be lightly crosslinked with formaldehyde vapor. The plug is normally formed cylindrically or as a composite in anticipation that a higher surface contact area will inhibit movement of the plug under arterial pressure. It is noteworthy that the bioresorption time of the plug can be controlled in part by varying the length of the plug, its bulk density, as well as the extent of crosslinking.

The environment surrounding a formed or forming thrombus influences its resolution. In the presence of flowing blood, the thrombus is in a state of flux

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with fresh platelets being deposited on the periphery, undergoing degranulation and thrombus enlargement. On the other hand, the flow of blood can dislodge weakly bound aggregates of platelets, thereby reducing the immediate size of the thrombus. In static blood, such as between two plugs, the number of platelets is fixed; whatever aggregation, degranulation and fibrin crosslinking that is going to take place will take place within 15 to 30 minutes after formation. From that point on, the thrombus will start to become remodeled by the action of plasmin and other proteases as well as by the invasion of migratory cells. In other words, resolution of the thrombus formed after placement of a single plug will be different from the resolution of the thrombi after placement of two plugs with a space therebetween. In the former configuration, fibroblast invasion and eventual blockage by replacement tissue will compete with the other processes as the thrombus is in a state of flux with access to fresh platelets. In the latter configuration, the two plugs are separated, permitting development of a solid tissue mass while protected from interference from the flux of blood. Thus, the plug 15, according to a second embodiment of the present invention, may be characterized as having two collagen pieces as described above and a spacer, or a bolus, of another material which is disposed between them for serving to separate them from each other. This material will remain localized between the two plug pieces for a desired period of time. A derivative of this two-piece design can include placement of an active agent into the space between the two plug pieces. This design can be optimized to manipulate the healing process. One embodiment of the plug assembly according to the invention involves insertion of a hyperosmotic agent

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spacer between the two plugs. The transient shock to the lumen of the vessel in the surrounding area could induce prolonged inflammation and enhance tissue fibrosis. Examples of such material include

5 concentrated salts or low molecular weight (such as less than 2000) polyethylene glycol which can act as a dehydrating agent at the occlusion site, influencing tissue remodeling. A bolus of radiopaque material held between the two plug pieces

10 will allow direct visualization of the occlusion site several days after surgery without the need for interventional techniques.

Another aggressive method of compromising the lumen in the space between the two plug pieces is by

15 introduction of surface active agents or alcohols into the spacer capsule. An alcohol may serve as a dehydrating agent, again compromising the cells and encouraging inflammation and the wound healing process. A surface active agent will effectively

20 destroy the epithelial layer, inducing inflammation and wound healing as above. Examples of surfactive agents include sodium tetradecyl sulfate and morrhuate sodium. This effect will probably be more prolonged than the osmotic and dehydration methods

25 explained above.

Although the plug 15 according to the present invention may be considered to serve primarily for occluding a tubular biological vessel such as a blood vessel, it can also itself provide supporting

30 chemotherapy to the site of occlusion by delivering various active agents to the site. In other words, collagen piece or pieces of the plug 15 may be pretreated with desirable clinical or therapeutic drugs such as clotting factors, tissue attachment

35 factors, chemotherapeutic agents, and anti-neoplastic

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agents. Thus, for example, chemotherapeutic agents may be slowly delivered to tissues downstream from the plug 15 as the plug 15 is bioresorbed. Fixation of drugs or other factors to the collagen structure

5 may be carried out by a variety of known methods, such as by treating the collagen with a solution of the drug or factor prior to drying and compressing the plug 15. The drugs or factors may be covalently bonded, ionically or hydrophobically bonded, or

10 merely physically absorbed into the collagen, depending upon the desired delivery profile of the drug because the mode of drug incorporation into the plug piece determines the release rate of the agent. Drugs or factors which are only physically absorbed

15 into the collagen will be almost instantaneously releasable as a bolus into the blood stream upon first contact with the blood, whereas drugs or factors which are covalently bonded to the collagen will be released over a prolonged period of time in

20 proportion with the time and degree of bioresorption of the collagen itself. Examples of active agents that may thus be incorporated include (1) antibiotics such as tobramycin, gentamycin, and vancomycin; (2) clotting factors such as Factors I-VIII, thrombin and

25 fibrinogen; (3) tissue attachment factors such as vitronectin, fibronectin and laminin; (4) protease inhibitors such as aprotinin and ethylenediaminetetraacetate (EDTA); (5) anti-neoplastic agents such as 5-fluorouracil,

30 methotrexate, nitroso-ureas, cisplatin, cyclophosphamide, dacarbazine, dactinomycin, doxorubicin, etoposide, mitomycin, vinblastine, and vindesine; and (6) sclerosing agents such as morrhuate sodium, ethanolamine oleate, and tetradecyl

35 sulfate.

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Next, a method will be explained for the use of a device of the type described above as an embolization device for a peripheral bypass or, more particularly, for an in-situ saphenous vein bypass graft in which the saphenous vein is transformed into an artery by stripping out the valves and connecting the proximal end to the femoral artery and the distal end to any combination of the infra-popliteal arteries.

According to one scenario, the angioscope is inserted from the proximal end of the vein. Valves are stripped by a usual procedure. The sheath assembly 20 is positioned in the opposite end of the vein from the angioscope in neighborhood of the branch vessel to be occluded. The user, while viewing the region through the angioscope, maneuvers the handle 42 to rotate the tip section 32 of the tube and to move the catheter 30 longitudinally such that its front opening 31 reaches into the desired side branch vessel. The touhy-Borst connector 24 is tightened to lock the catheter position relative to the sheath. Once the user is satisfied that the front opening 31 is inside the desired side branch vessel by using the indicator lines 33 on the catheter as reference, the plunger body 43 is rotated to unlock it and is then pushed forward, thereby advancing the push rod 50 forward and compressing the helical spring 46. As soon as it is ascertained that the plug 15 has been discharged from the catheter 30 and deposited at a target site in the vessel, the user releases the plunger body 43, causing the push rod 50 to retract immediately by the restoring force of the compressed spring 46. This serves to prevent inadvertent infliction of damage to the vessel by the push rod 50.

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Although the present invention has been described above with reference to only one device as an example and its use in a saphenous vein bypass graft procedure, this example is intended to be merely
5 illustrative, and not as limiting the scope of the invention. Many modifications and variations are possible within the spirit of the present invention. For example, Fig. 7 shows another sheath assembly 120 embodying the present invention, which may be
10 considered a variation of the embodiment described above with reference to Fig. 2. For the convenience of disclosure, therefore, components which are at least similar to those described above are indicated in Fig. 7 by numerals with the same lower two digits,
15 such as a sheath tubing 122 bonded to the distal end of a hemostasis fitting 121. For the sake of clarity, the catheter 30 is omitted from Fig. 7.

The modified sheath assembly 120 shown in Fig. 7 is characterized in that the hemostasis fitting 121 is
20 locked onto the distal end of a T-connector 127 by means of a locking member 128 and that the proximal end of the T-connector 127 is screwed onto a Touhy-Borst connector 124. An irrigation port 126 connected to a pigtail irrigation line 129 is screwed
25 onto the T-connector 127 such that a stream of fluid can be caused to exit through an annular space between the sheath tubing 122 and the catheter (not shown) passed therethrough.

Another plug-delivering device embodying the present
30 invention, which incorporates the sheath assembly 120 of Fig. 5 and may be considered a stripped-down version of the device described with reference to Figs. 1-6, may be characterized also as having a simplified deployment assembly (not separately shown)
35 structured substantially as shown in Fig. 6, the

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proximal end of the catheter (not shown) being bonded directly to the distal end of the handle 42. In other words, this simplified stripped-down version of the device does not have the capability of irrigating
5 through the catheter tip.

Figs. 8A, 8B and 8C show alternative designs for the front end section 32 of the catheter 30. The embodiment shown in Fig. 8A is characterized as having the tip integrally formed with the catheter
10 tubing and holding a straight ferrule 35. Fig. 8B shows an embodiment with a ferrule 35 made, for example, of stainless steel and having a brim 36 with rounded edges around the front opening 31. Fig. 8C shows an embodiment with a lower durometer
15 unreinforced tip 34 which is bonded to the distal end of reinforced catheter tubing. Instead of a ferrule, a liner 35 is provided on the inner surface of the tip 34, having a brim 36 with rounded edges around the front opening 31 like the ferrule 35 shown in
20 Fig. 8B.

As a further variation, the front opening of the tip section of the catheter may be provided with a lid such that the plug loaded therein may be kept dry and away from body fluid. Fig. 11 shows the distal end
25 of such a catheter, characterized as having an end cap 60 permanently affixed to its front end for retaining a slit valve 61 adapted to prevent body fluids such as blood from entering the interior of the catheter through the end cap 60. As shown, the
30 slit valve 61 according to a preferred embodiment of the invention is tricuspid and is deformable by way of its three flaps 62 which allow passage therethrough of an object within the catheter if an appropriate outward force is applied thereon. Figs.
35 10A and 10B show sectional views of the front end of

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this catheter respectively when a dry compressed plug 63 (such as one of the collagen plugs described above) is kept completely inside the catheter behind the slit valve 61 and when the plug 63 is being
5 delivered out of the catheter through the slit valve 61 by a force applied thereon by the push rod 50. Although not necessary, the plug 63 is shown in Figs. 10A and 10B as having a slightly rounded front end so as to assist smooth delivery through the slit valve
10 61. The end cap 60 may be made of any nontoxic material such as plastic or nontoxic metal. According to a preferred method of fabrication, the end cap 60 and the slit valve 61 are formed as one piece in a mold such that there is initially a
15 central plastic membrane surrounded by an annular housing to serve as the cap 60. The membrane is thereafter incised to form the flaps 62 of the slit valve 61. Since the slit valve 61, for sanitary reasons, is normally not intended to be used more
20 than once, it is not necessary that the flaps 62 return to their original closed positions after they are deformed once to let the plug 63 pass through. If these flaps 62 remain deformed after the plug 63 has been expelled, body fluids can still be prevented
25 from entering the catheter by properly designing the sheath assembly 20, as explained above with reference to Fig. 2. On the other hand, it may be advantageous to make the flaps 62 sufficiently thick and resilient such that they return to their original closed
30 positions after they allow the plug 63 to pass therethrough because it may be clinically necessary or desirable in some instances to deliver more than one plug into the blood vessel. In such an instance, more than one plug may be loaded into the catheter
35 before the plunger head 64 is inserted into the catheter. Alternatively, a single plug may be inserted and, once inserted, the plunger head 64 may

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be withdrawn while still retaining the catheter in the blood vessel. Another plug may then be loaded into the catheter and the plunger head 64 may be reinserted for delivering the next plug.

- 5 Although the device was described above as consisting of three parts, it was merely for the convenience of description. The catheter, for example, may be considered a part of the deployment assembly. In summary, all such modifications and variations of the
- 10 disclosure given above, that may be apparent to a person skilled in the art, are intended to be included within the scope of the invention.

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WHAT IS CLAIMED IS:

1. A device for delivery of an embolization plug into a biological vessel, said device comprising:
a tubular sheath assembly having a proximal
5 opening and a distal opening connected by a passage;
a flexible tube disposed through said passage and having a proximal end section and a distal end section, said distal end section being adapted to hold said embolization plug therein, extending out of
10 said distal opening of said sheath assembly and being naturally arcuate, wherein the curvature of said distal end section can be changed by moving said tube longitudinally through said passage; and
an elongated plunger disposed slidably inside said
15 tube and having a back end and a front end, said front end serving to push said embolization plug out of said tube.
2. The device of claim 1 wherein said distal end section is substantially semicircular when
20 unconstrained, and the curvature thereof can be reduced as said tube is pulled towards said proximal end section to thereby reduce the distance by which said distal end section extends out of said distal opening of said sheath assembly.
- 25 3. The device of claim 2 wherein said distal end section has a radius of curvature of about 1.6-6.4mm when unconstrained.
4. The device of claim 1 wherein said tube is capable of translating a torque exerted thereon at
30 said proximal end section to said distal end section, wherein said distal end section can be controllably rotated by applying a torque on said tube at said proximal end section.

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5. The device of claim 1 wherein said tube comprises a material selected from the group consisting of polyurethane, polyethylene, polypropylene, polyamide, polyvinyl chloride, polyether block amide, fluoropolymers, and polyetheretherketone.

6. The device of claim 5 wherein said tube further comprises a reinforcing material capable of preventing said tube from elongating axially and of providing torqueability.

7. The device of claim 1 wherein said plunger has at said front end a plunger head which is sufficiently flexible so as to be able to move inside, and without significantly interfering with, the arcuate configuration of said distal end section of said tube.

8. The device of claim 7 wherein said plunger comprises a wire of variable stiffness and a metal safety ribbon that are soldered to an outer helical wire winding that is coated with a lubricious material.

9. The device of claim 1 further comprising a plug-deploying means for allowing a user to operate thereon to thereby cause said plunger to push said plug out of said tube, said plug-deploying means being attached to said back end of said plunger.

10. The device of claim 9 wherein said plug-deploying means includes a spring which increases its biasing force as said plug-deploying means is operated to push said plug out of said tube.

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11. The device of claim 9 wherein said plug-deploying means includes an inlet for introducing a liquid directed into said tube.

12. The device of claim 1 wherein said sheath
5 assembly includes tube-grasping means for grasping said tube from outside so as to prevent air and liquid from passing thereacross through space between said tube and said sheath assembly.

13. The device of claim 1 wherein said sheath
10 assembly includes a port for introducing liquid between said sheath assembly and said tube.

14. The device of claim 1 wherein said distal end
section of said tube includes a slit valve for
preventing body fluids from entering the interior of
15 said tube.

15. The device of claim 14 wherein said slit
valve includes deformable flaps adapted to be
deformed as said plug is pushed out of said tube by
said plunger.

16. The device of claim 1 wherein said distal end
20 section of said flexible tube contains a ferrule for holding said plug therein, said ferrule having an inner surface with low coefficient of friction.

17. The device of claim 16 wherein said ferrule
25 has a brim which is exposed externally and has rounded edges.

18. The device of claim 1 wherein said distal end
section of said flexible tube includes a lower
durometer reinforced tubular member bonded to said
30 flexible tube and a liner on the inner surface of

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said tubular member, said liner having a brim which is exposed externally and has rounded edges.

19. A device for delivery of an embolization plug into a biological vessel, said device comprising:

- 5 a tubular sheath assembly having a proximal opening and a distal opening connected by a passage;
a flexible tube disposed through said passage and having a proximal end section and a distal end section, said distal end section being adapted to
10 hold said embolization plug therein, extending out of said distal opening of said sheath assembly;

- an elongated plunger disposed slidably inside said tube and having a back end and a front end, said front end serving to push said embolization plug out
15 of said tube; and

a plug-deploying means for allowing a user to operate thereon to thereby cause said plunger to advance through said tube by no more than a limited distance.

- 20 20. The device of claim 19 wherein said limited distance is such that said front end of said plunger is prevented from protruding out of said tube by more than a specified maximum distance.

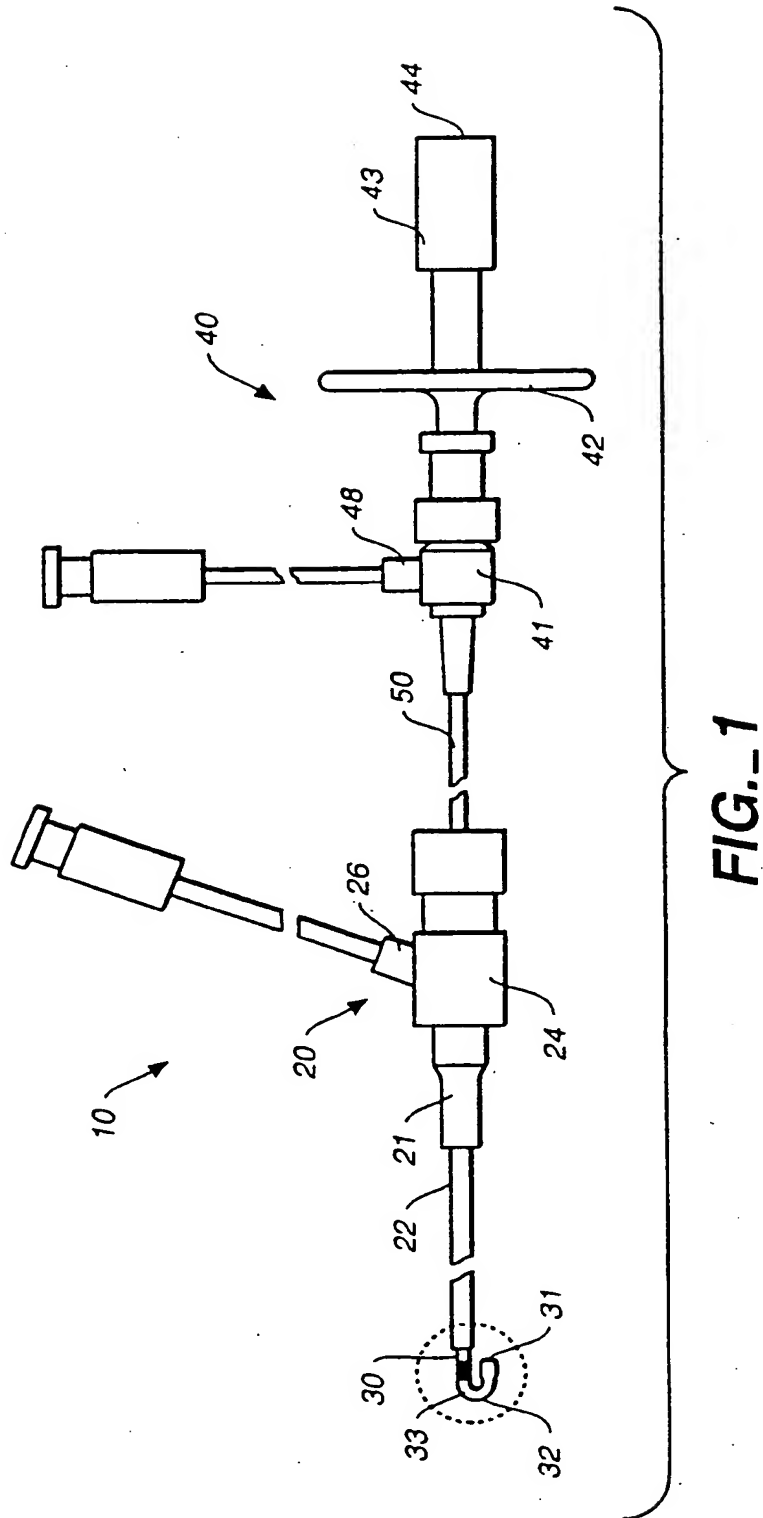
21. The device of claim 19 wherein said tube
25 comprises a material selected from the group consisting of polyurethane, polyethylene, polypropylene, polyamide, polyvinyl chloride, polyether block amide, fluoropolymers, and polyetheretherketone.

- 30 22. The device of claim 21 wherein said tube further comprises a reinforcing material capable of preventing said tube from elongating axially and of providing torqueability.

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23. An embolization device for a biological vessel, said device comprising:

- a plug adapted to be deposited in said vessel;
- a tubular sheath assembly having a proximal
- 5 opening and a distal opening connected by a passage;
- a flexible tube disposed inside said passage and having a proximal end section and a distal end section, said distal end section containing said plug therein, extending out of said distal opening of said
- 10 sheath assembly and being naturally arcuate, wherein the curvature of said distal end section can be changed by moving said tube longitudinally through said passage; and
- an elongated plunger disposed slidably inside said
- 15 tube and having a back end and a front end, said front end serving to push said plug out of said tube.



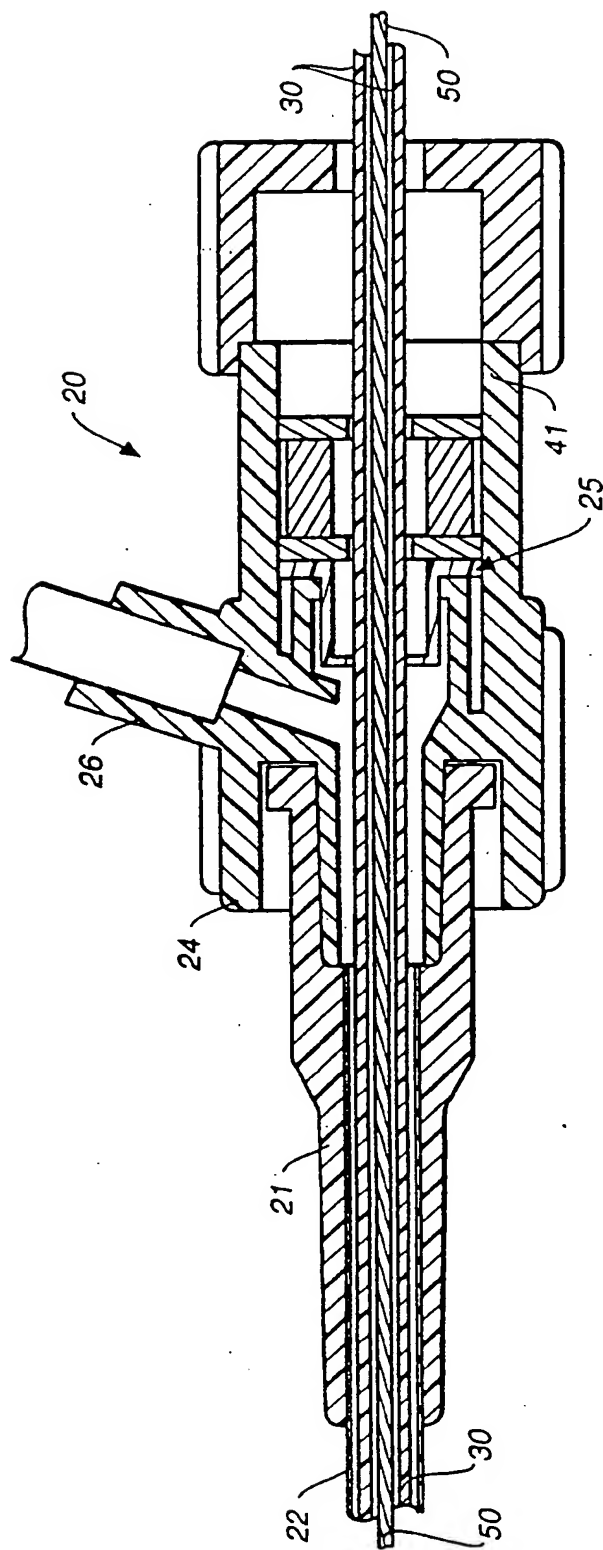
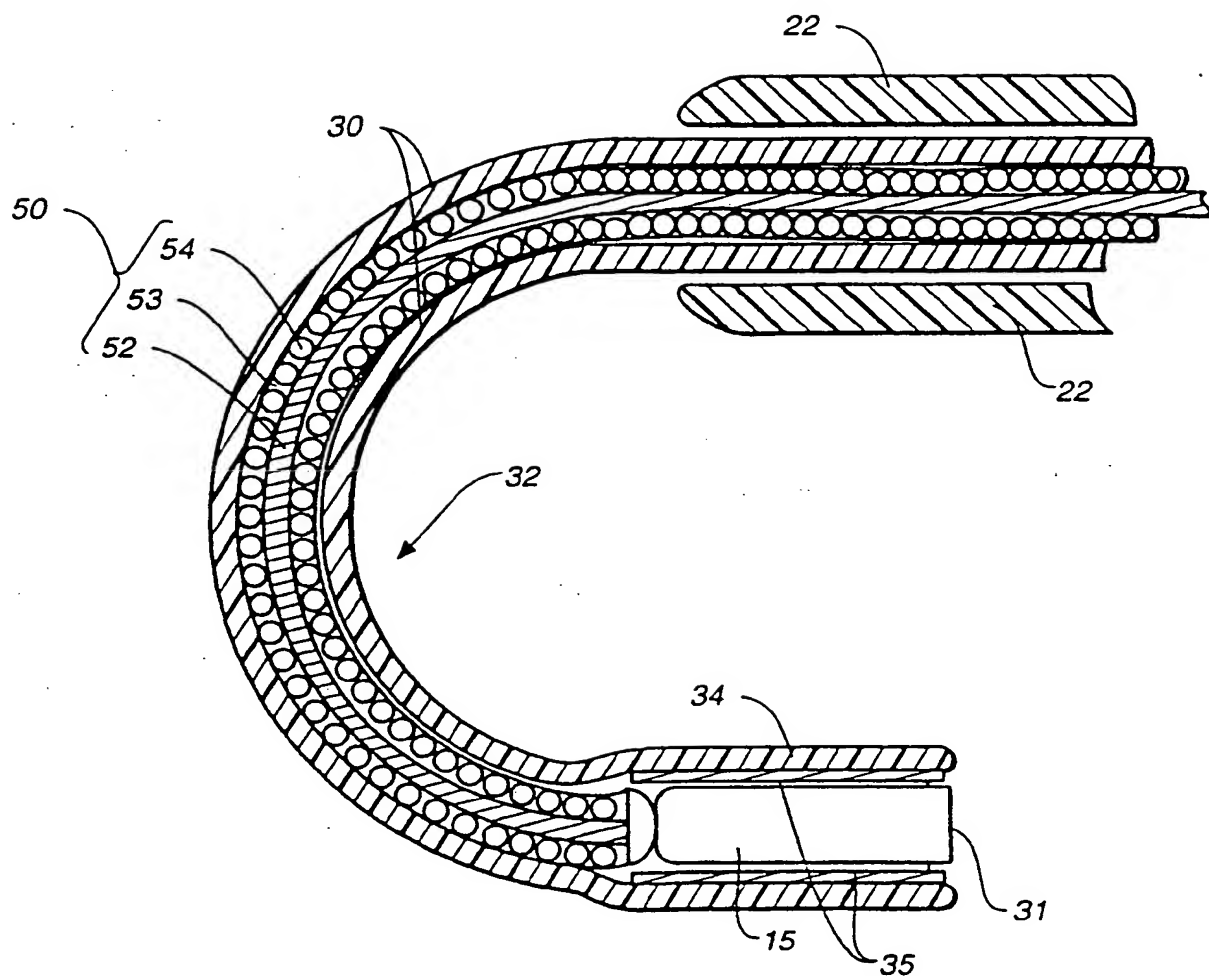
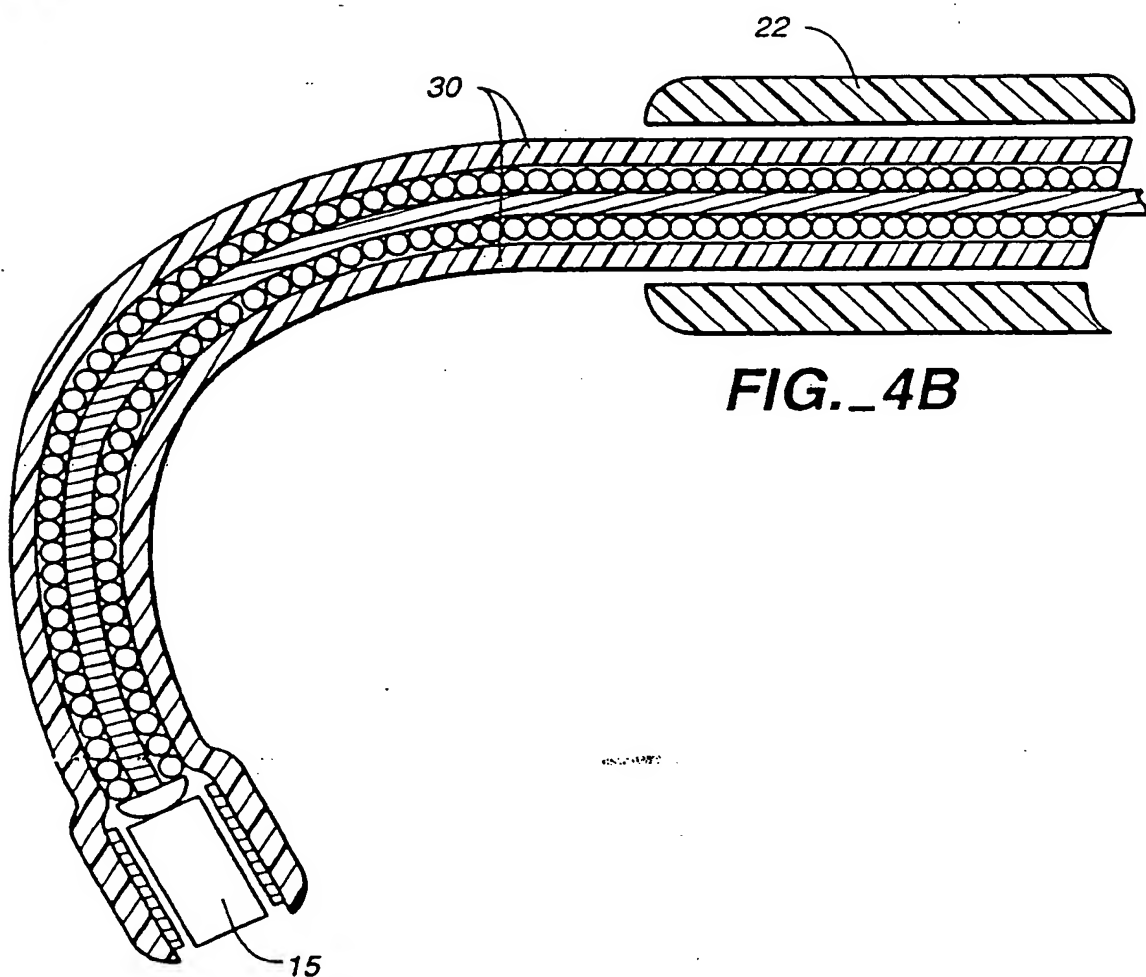
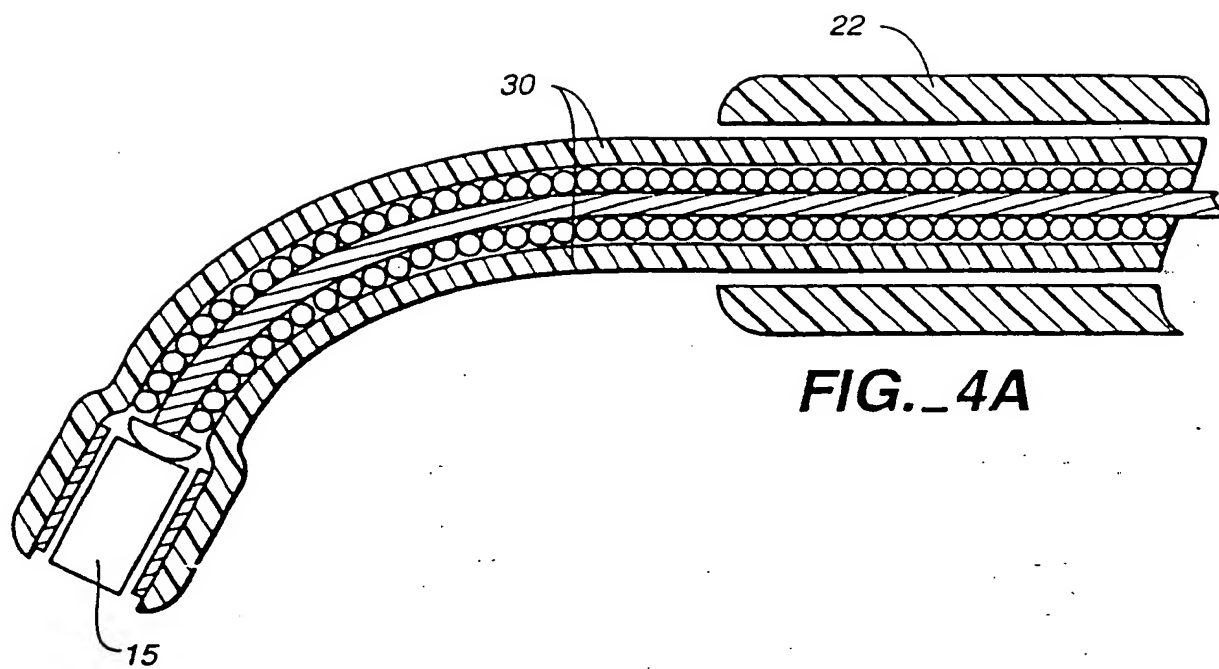
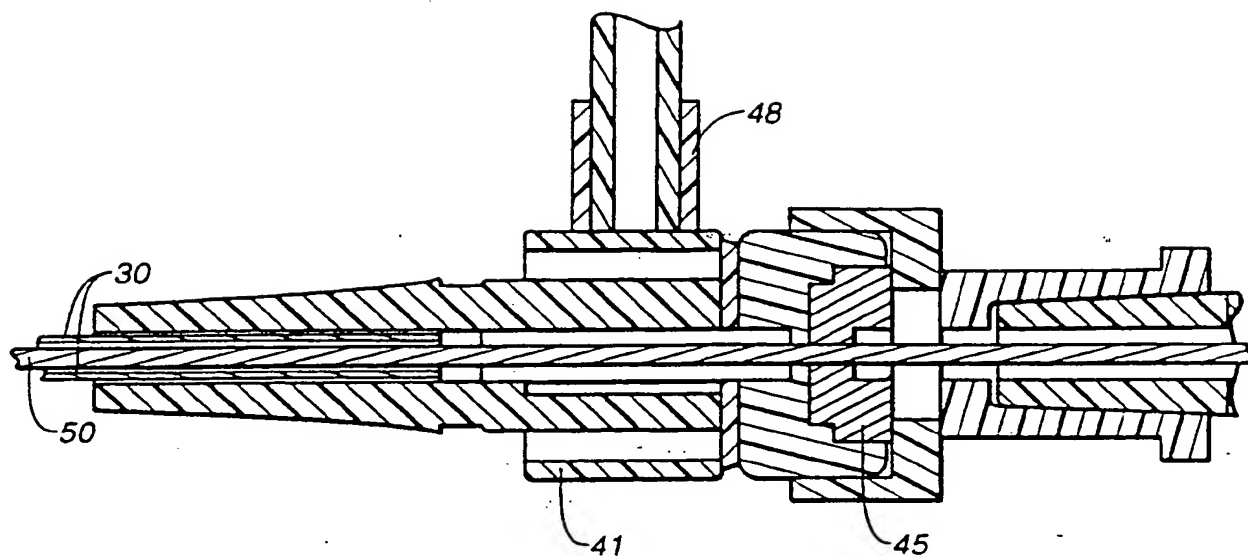
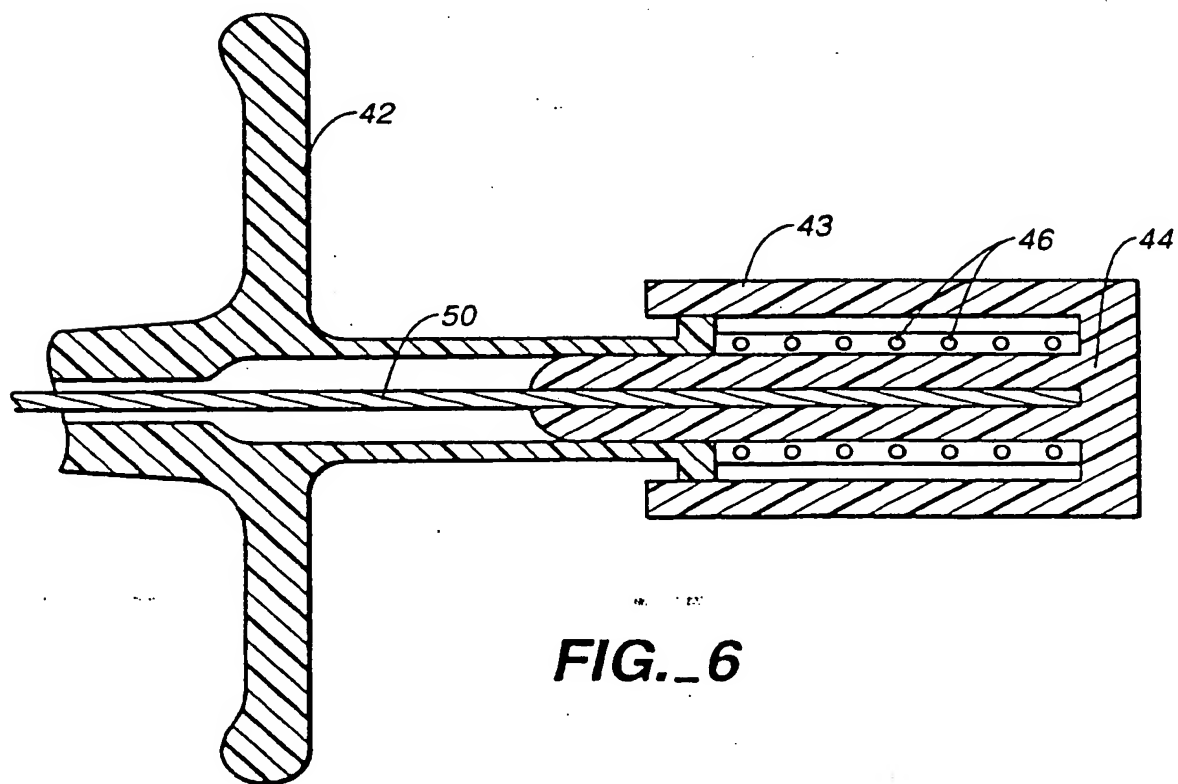


FIG. 2

**FIG. 3**



**FIG._5****FIG._6**

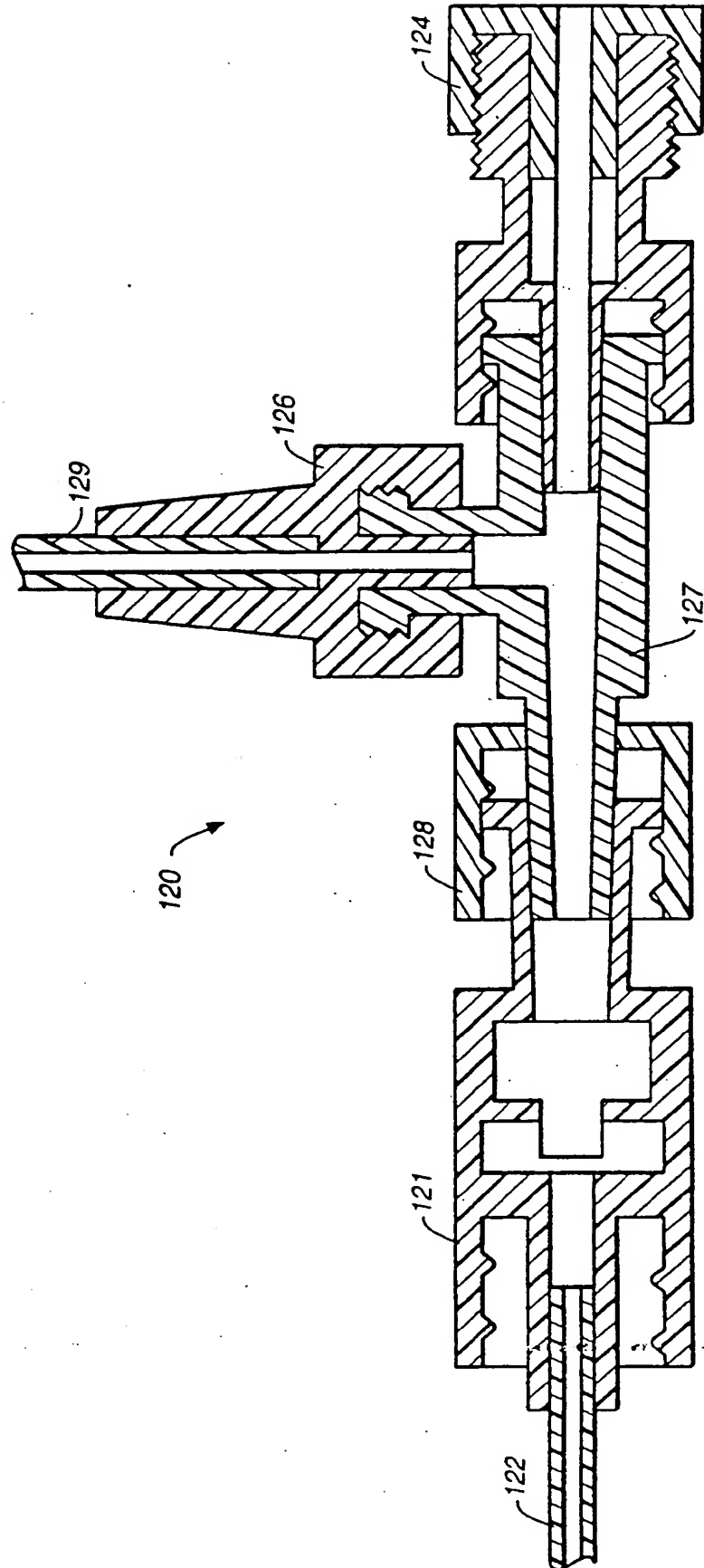


FIG. 7

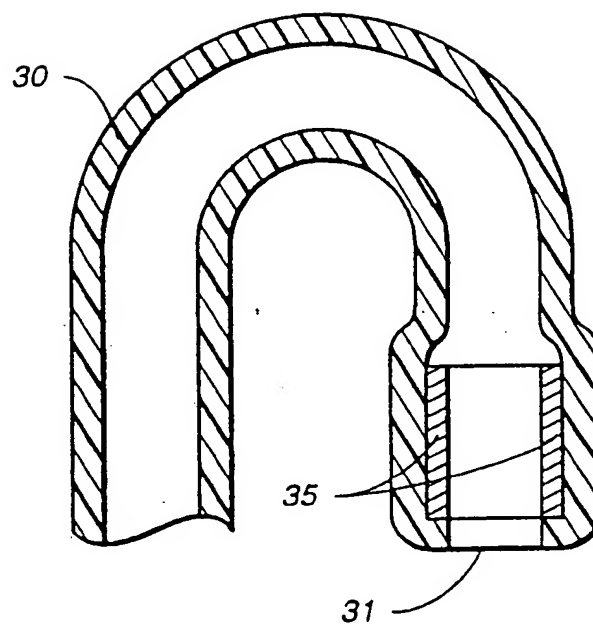


FIG. 8A

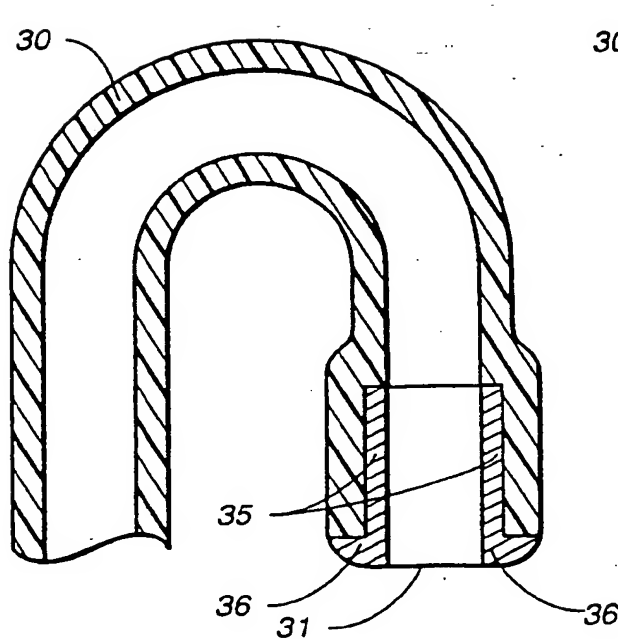


FIG. 8B

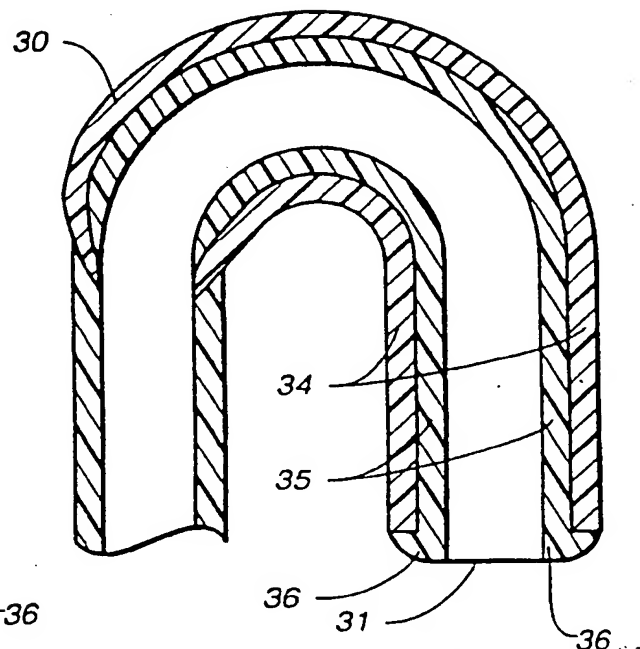
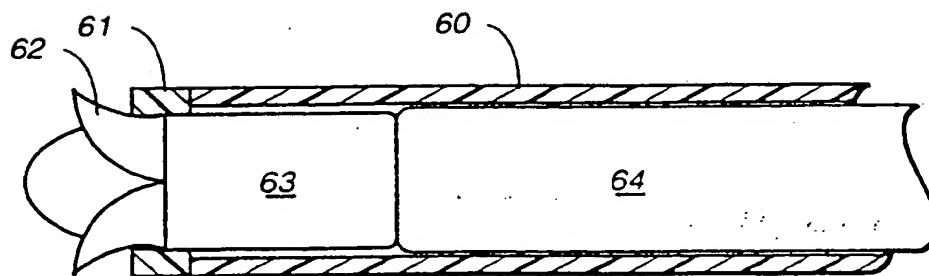
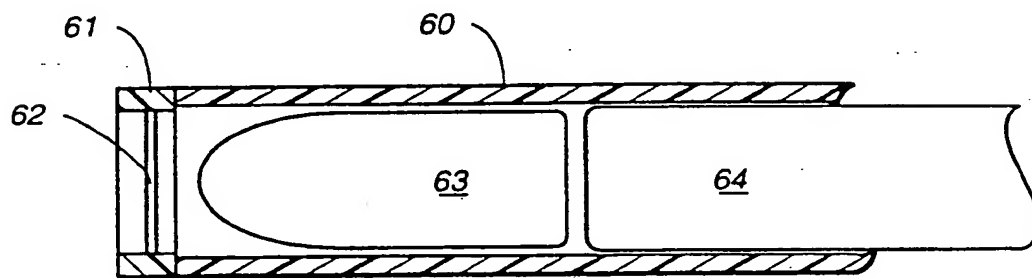
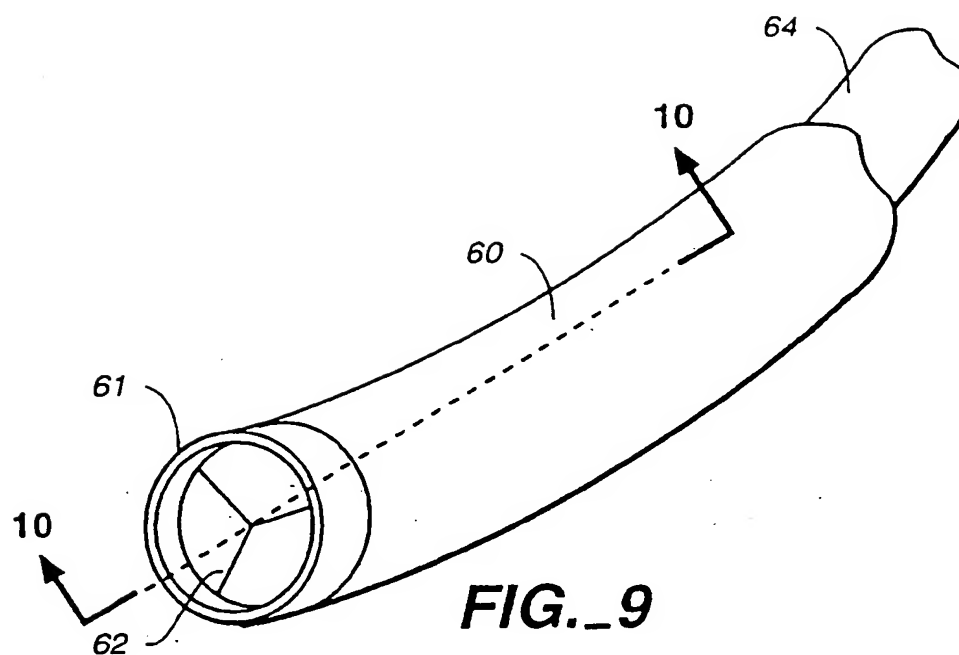


FIG. 8C

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INTERNATIONAL SEARCH REPORT

Inter. nal Application No
PCT/US 94/05079

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 A61B17/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 A61B A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US,A,5 061 274 (KENSEY) 29 October 1991 see column 5, line 33 - column 6, line 11; figures 4,5 ---	1,19,23
Y	US,A,5 084 012 (KELMAN) 28 January 1992 see column 3, line 4 - line 54; figures 2,3 ---	1,23
Y	FR,A,2 641 692 (NIPPON) 20 July 1990 see page 18, line 5 - line 17; figure 28 ---	19
A	FR,A,2 573 986 (MEDIVENT) 6 June 1986 see abstract see page 13, line 20 - page 14, line 2; figure 5 --- -/--	1,23

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

24 August 1994

Date of mailing of the international search report

13. 09. 94

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INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/US 94/05079

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>US,A,5 167 624 (BUTLER ET AL.) 1 December 1992 see column 6, line 42 - line 65; figures 1,3,4 -----</p>	1,23

INTERNATIONAL SEARCH REPORT

information on patent family members

Inter nal Application No

PCT/US 94/05079

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US-A-5061274	29-10-91	WO-A- 9307813 US-A- 5192302	29-04-93 09-03-93
US-A-5084012	28-01-92	CA-A- 2106865 EP-A- 0576465 WO-A- 9216246	23-09-92 05-01-94 01-10-92
FR-A-2641692	20-07-90	JP-A- 2277459 US-A- 5192301	14-11-90 09-03-93
FR-A-2573986	06-06-86	AU-B- 584967 AU-A- 5232186 CA-A- 1294392 CH-A- 671875 DE-T- 3590638 EP-A, B 0236333 GB-A- 2191097 JP-T- 62501271 WO-A- 8603398 US-A- 4732152	08-06-89 01-07-86 21-01-92 13-10-89 10-12-87 16-09-87 09-12-87 21-05-87 19-06-86 22-03-88
US-A-5167624	01-12-92	NONE	